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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,202	04/13/2006	Osamu Honmou	033873-0108	4131

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EXAMINER	
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ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,202	HONMOU ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,8,9 and 11-30* is/are pending in the application.

4a) Of the above claim(s) *20-22,25 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,8,9,11-19,23,24 and 26-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/13/2009 has been entered.

Claim Status

Claims 6, 8, 9 and 11-30 are pending. Claims 1-5, 7 and 10 are cancelled. Claims 6, 8-9 and 11-19 are amended. Claims 29-30 are newly submitted. However, claims 20-22, 25 and 28-30 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim (see Restriction section below). Claims 6, 8, 9, 11-19, 23-24 and 26-27 are under current examination.

Priority

This application claims benefit as a 371 National Stage application of PCT/JP04/09386 (filed 06/25/2004). The application also claims benefit from foreign application, JAPAN 2003-432329 (filed 12/26/2003). However, the applicant has not

submitted a certified copy of JAPAN 2003-432329. Therefore, the applicant has not fulfilled the requirements of 35 USC 119 (a)-(d). Although the applicant has submitted a certified translation of JAPAN 2003-432329, this is not the same as a certified copy as required by 35 USC 119 (a)-(d), in order to be afforded the benefit of the filing date of JAPAN 2003-432329. Therefore, the instant application has been granted the benefit date, 25 June 2004, from the application PCT/JP04/09386.

Election/Restrictions

Newly submitted claims 29-30 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 29-30 are directed to a method of treating brain tumors. The applicant has traversed the pending restriction. The applicant suggests the broadened scope of claims 6 and 9 has removed the burden of examination. As explained in the last action, the originally examined claims contained a product and a method of treating a cranial nerve disease. Upon introduction of claims directed to a method of treating brain cancer, the examiner withdrew such claims because there is a search burden. Prior art directed to treating stroke with mesenchymal cells would not overlap with prior art directed to treating brain cancer with mesenchymal cells. The examiner provided art (Twardzik or Mahmood) which anticipated the original claims, thereby demonstrating lack of unity. In addition, as a national stage application of PCT/JP04/09386, the applicant is not entitled to a second method of using, and restriction is proper according to 37 CFR § 1.475 (d):

Unity of invention before the International Searching Authority, the International Preliminary Examining Authority and during the national stage.

> (a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.
>
> **(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:**
>
> (1) A product and a process specially adapted for the manufacture of said product; or
> (2) A product and process of use of said product; or
> (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
> (4) A process and an apparatus or means specifically designed for carrying out the said process; or
> (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.
>
> **(c) If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present.**
>
> (d) If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and § 1.476(c).

Therefore, the examiner maintains the withdrawal of claims 20-22, 25 and 28. Furthermore, because claims 29-30 are directed to said second method of using (i.e., treating brain cancer), the examiner further withdraws claims 29-30.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 20-22, 25 and 28-30 are withdrawn from

consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. The restriction is hereby made final.

RESPONSE TO ARGUMENTS

35 USC § 112, 1st paragraph (New Matter)

Claim amendments, filed 13 April 2009, with respect to claim 17 has been fully considered and are persuasive. The rejection of Claim 17 under 35 USC 112, first paragraph, has been made moot by the claim amendments submitted on 13 April 2009 and is hereby withdrawn.

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Mahmood

Claims 9, 11-15 and 17-19 remain rejected under 35 USC 102(b) as anticipated over Mahmood et al. (Neurosurgery, Vol.49, No.5, November 2001: 1196-1204) for the reasons of record and the comments below.

Applicant's arguments and claim amendments filed 13 April 2009 have been fully considered but they are not persuasive.

The applicant argues that the cells of Mahmood et al. are not the same as those used in the instant application. The applicant argues "the 'marrow stromal cells' described by Mahmood et al….and the 'mesenchymal stem cells' of the present invention are distinct cell populations" (Remarks, page 8). The examiner finds this argument unpersuasive. Mahmood et al. teach “stem cells for non-hematopoietic tissues are…referred to as marrow stromal cells (MSCs). MSCs are multipotent and can differentiate into…brain cells” (Page 1196, col.1.). In addition, the examiner notes that the art often refers to mesenchymal stem cells as marrow stromal cells. Therefore, the examiner finds the applicant's argument unpersuasive.

Accordingly, the applicant hereby maintains the rejection of claims 9, 11-15 and 17-19 under 35 USC 102(b) as anticipated by Mahmood et al. (Neurosurgery, Vol.49, No.5, November 2001: 1196-1204).

The examiner reiterates the pending rejection:

Claims 9, 11-15 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Mahmood et al (Neurosurgery, Vol.49, No.5, November 2001: 1196-1204).

Claim 9 is directed to a method for treating a cranial nerve disease comprising the in vivo administration to a patient of a therapeutically effective amount of a cranial nerve disease therapeutic agent for in vivo administration, comprising a mesenchymal cell as an active ingredient. Mahmood et al. teach “stem cells for non-hematopoietic

tissues are…referred to as marrow stromal cells (MSCs). MSCs are multipotent and can differentiate into…brain cells" (Page 1196, col.1.). In addition, the examiner notes that the art often refers to mesenchymal stem cells as marrow stromal cells. Mahmood et al. teach, "transplantation studies in cerebral ischemia, functional outcome was significantly improved in MSC-transplanted rats compared with bone marrow-transplanted animals….Bone marrow or MSCs transplanted directly into the striatum and cortex of rat brain subjected to TBI or middle cerebral artery occlusion migrate…induce neurological and functional improvement… Intravenous transplantation has the advantage of carrying the cells over a much wider area." (page 1196, col.2). MSC is an acronym for marrow stromal cells. Mesenchymal progenitor cells are components of bone marrow stroma. Mahmood et al. specifically describe mesenchymal cells administered by IV methods (page 1200, col.2).

The specification states, "the term 'mesenchymal cells' preferably refers to, for example, bone marrow cells (mononuclear cell fraction of bone marrow cells; MCF (mononuclear cell fraction)), cord blood cells, peripheral blood cells, mesenchymal stem cells (MSCs), or cells derived from these cells." (page 5, lines 30-32). The specification further indicates that "mesenchymal stem cells may differentiate…via stromal cells into nerves" (page 6, lines 6-8). Because the specification indicates that marrow stromal cells are derived from mesenchymal stem cells, the examiner believes the teachings of Mahmood et al. satisfy the limitation of "mesenchymal cells" as taught by the specification.

Claim 11 is directed to the method of claim 9 , wherein the cranial nerve disease is cerebral infarction. The examiner believes Mahmood's treatments of the cerebral artery occlusion satisfy this claim.

Claim 12 is directed to the method of claim 9, wherein the in vivo administration is intravenous administration. Mahmood et al. specifically describe mesenchymal cells administered by IV methods (page 1200, col.2).

Claim 13 is directed to the method of claim 9, wherein the mesenchymal cell is a bone marrow cell, a cord blood cell, or a peripheral blood cell. Mahmood et al. teach mesenchymal cells from bone marrow.

Claim 14 is directed to the method of claim 13, wherein the bone marrow cell is an autologous cell of the patient. Mahmood et al. teach autologous MSCs (page 1200, col.2).

Claim 15 is directed to the method of claim 11, wherein the severe cerebral infarction is in a hyper acute stage of an acute stage. The specification does not define acute or hyperacute stage cerebral infarction. Therefore, the examiner asserts that Mahmood's treatments the cerebral artery occlusion satisfy this limitation of claim 15.

Claim 17 is directed to the method of claim 11, wherein the cranial nerve disease therapeutic agent is administered to a patient at any one of the times selected from:…a) within 72 hours from the onset of a cerebral infarction of a several cerebral infarction. Mahmood et al. teach administration of mesenchymal cells 24 hours after traumatic brain injury (abstract).

Claim 18 is directed to a method for neuroprotection of a cranial nerve disease patient comprising in vivo administration to a patient of a therapeutically effective amount of an agent comprising a mesenchymal cell as an active ingredient. The specification suggests that examples of cranial nerve diseases include "cerebral infarction, spinal cord injuries and demyelinating diseases" (page 4, lines 1-2). The examiner believes Mahmood's description of transplantation of mesenchymal cells into rat brains affected by cerebral artery occlusion satisfy this claim.

Claim 19 is directed to a method for regenerating the cranial nerve of a cranial nerve disease patient comprising the in vivo administration to a patient of a therapeutically effective amount of an agent comprising a mesenchymal cell as an active ingredient. Mahmood et al. teach "survival and growth of the graft within the brain" (page 1196, col.2).

Accordingly, Mahmood et al. anticipated the instant claims.

Gold

The rejection of claims 6 and 8 under 35 USC 102(b) as anticipated over Gold et al. (US2002/0168766, published 14 November 2002) is withdrawn in response to the applicant's arguments and/or claim amendments.

The applicant's arguments have been fully considered and are persuasive. The applicant has amended the claims so that the claims specifically recite "mesenchymal stem cell." The teachings of Gold differ from the instant claims only in that the cells of

Gold are pluripotent stem cells. The examiner deems this difference sufficient to overcome the pending rejection.

Therefore, the examiner hereby withdraws the rejection of claims 6 and 8 under 35 USC 102(b) as anticipated over Gold et al.

Kazuhiko

Claims 6, 8, 9, 11-13, 15-19, 23-24 and 26-27 remain rejected under 35 USC 102(a) as anticipated by Kazuhiko et al (Molecular Therapy. Feb 2004. 9(2): 189-197) for the reasons of record and the comments below.

Applicant's arguments filed 13 April 2009 have been fully considered but they are not persuasive.

The applicant argues Kazuhiko et al. is not properly considered prior art. The applicant argues that the present application should properly be granted the benefit of Japanese priority application, JAPAN 2003-432329. The examiner finds this argument unpersuasive, because the instant application has not complied with the requirements of 35 USC 119 (a)-(d), regarding submission of a certified copy of Japanese priority application, JAPAN 2003-432329. Accordingly, the present application has not been granted a benefit date which would permit withdrawal of Kazuhiko as prior art. Therefore, the examiner maintains the pending rejection.

The examiner reiterates the pending rejection below:

Claims 6, 8-9, 11-13, 15-19, 23-24 and 26-27 are rejected under 35 U.S.C. 102(a) as being anticipated by Kazuhiko et al (Molecular Therapy. Feb 2004. 9(2): 189-197).

Claim 6 is directed to a cranial nerve disease therapeutic agent for in vivo administration, comprising a mesenchymal stem cell as an active ingredient, wherein the mesenchymal stem cell is: (a) a mesenchymal stem cell that has been treated *ex vivo* with a transfection vector comprising a BDNF gene, PLGF gene, GDNF gene, or IL-2 gene; or (b) an immortalized mesenchymal stem cell that has been treated *ex vivo* with a transfection vector comprising an hTERT gene. Kazuhiko et al. teach administration of "transfected…human MSC [mesenchymal stem cells] with the BDNF gene…contributed to improved functional recovery in a rat…MCAO model" (abstract). Kazuhiko et al. use mesenchymal stem cells in their method.

Claim 8 is directed to the agent of claim 6, wherein the mesenchymal stem cell is a bone marrow cell, a cord blood cell, or a peripheral blood cell. Kazuhiko et al. teach their mesenchymal stem cell are bone marrow stromal cells.

Claim 9 is directed to a method for treating a cranial nerve disease comprising the in vivo administration to a patient of a therapeutically effective amount of a cranial nerve disease therapeutic agent for in vivo administration, comprising a mesenchymal stem cell as an active ingredient. Kazuhiko et al. teach administration of "transfected…human MSC [mesenchymal stem cells] with the BDNF gene…contributed to improved functional recovery in a rat…MCAO model" (abstract).

Claim 11 is directed to the method of claim 9 , wherein the cranial nerve disease is cerebral infarction. Kazuhiko et al. teach a rat model of transient Middle Cerebral Artery Occlusion (abstract).

Claim 12 is directed to the method of claim 9, wherein the in vivo administration is intravenous administration. Kazuhiko et al. teach intravenous administration of MSC.

Claim 13 is directed to the method of claim 9, wherein the mesenchymal cell is a bone marrow cell, a cord blood cell, or a peripheral blood cell. Kazuhiko et al. teach mesenchymal cells from bone marrow.

Claim 15 is directed to the method of claim 11, wherein the severe cerebral infarction is in a hyper acute stage of an acute stage. The specification does not specifically define acute or hyperacute stage cerebral infarction. Therefore, the examiner asserts that Kazuhiko's treatments of the cerebral artery occlusion satisfy this limitation of claim 15.

Claim 16 is directed to the method of claim 9, wherein the mesenchymal stem cell is: (a) a mesenchymal stem cell that has been treated *ex vivo* with a transfection vector comprising a BDNF gene, PLGF gene, GDNF gene, or IL-2 gene; or (b) an immortalized mesenchymal cell that has been treated *ex vivo* with a transfection vector comprising an hTERT gene. Kazuhiko et al. teach administration of "transfected…human MSC [mesenchymal stem cells] with the BDNF gene…contributed to improved functional recovery in a rat…MCAO model" (abstract). The transfection of MSC was performed *in vitro* prior to transplantation (page 195, col.2, Adenovirus infection).

Claim 17 is directed to the method of claim 11, wherein the cranial nerve disease therapeutic agent is administered to a patient at any one of the times selected from:…a) within 72 hours from the onset of a cerebral infarction of a several cerebral infarction. Kazuhiko et al. teach administration of mesenchymal stem cells 24 hours after MCAO (page 196, col.1).

Claim 18 is directed to a method for neuroprotection of a cranial nerve disease patient comprising in vivo administration to a patient of a therapeutically effective amount of an agent comprising a mesenchymal stem cell as an active ingredient. The specification suggests that examples of cranial nerve diseases include "cerebral infarction, spinal cord injuries and demyelinating diseases" (page 4, lines 1-2). The examiner believes Kazuhiko's description of transplantation of mesenchymal stem cell into rat brains affected by cerebral artery occlusion satisfy this claim.

Claim 19 is directed to a method for regenerating the cranial nerve of a cranial nerve disease patient comprising the in vivo administration to a patient of a therapeutically effective amount of an agent comprising a mesenchymal stem cell as an active ingredient. Kazuhiko et al. teach "functional recovery" of rats treated with MSC-BDNF, which also produced nerve growth factors and promotes "neuroprotective responses". (abstract and page 190, col.1).

Claim 23 is directed to a method for delivering therapeutic genes to a neurological disease site of a patient with neurological disease, comprising the in vivo administration of a therapeutically effective amount of mesenchymal stem cells to a patient in need thereof. Kazuhiko et al. teach administration of "transfected…human

MSC [mesenchymal stem cells] with the BDNF gene…contributed to improved functional recovery in a rat…MCAO model" (abstract).

Claim 24 is directed to the method of claim 23, wherein the neurological disease is cerebral infarction. The model used by Kazuhiko et al. is a model of cerebral infarction.

Claim 26 is directed to the method of claim 24, wherein the in vivo administration is intravenous administration. Kazuhiko et al. teach IV administration (page 190, col.1).

Claim 27 is directed to the method of claim 25, wherein the in vivo administration is direct administration. Kazuhiko et al. teach intraparenchymal administration (page 190, col.1).

Accordingly, Kazuhiko et al. anticipated the instant claims.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Scott Long/
Patent Examiner, Art Unit 1633